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BORDEN'S REVIEW of NUTRITION RESEARCH

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Summaries and reviews of research information concerning the nutritive values of milk and milk products. Published by The Borden Company, 350 Madison Avenue, New York, N. Y.

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Purpose of Borden's Review of Nutrition Research

This is the first issue of BORDEN'S REVIEW OF NUTRITION RESEARCH. The Review will be published to keep members of the Borden personnel and others who may be interested informed on new developments in nutrition research, particularly as related to milk and milk products, universally recognized as the foundation components of good diets for persons of all ages.

This issue of the Review begins a series of articles the timely purpose of which is to present the facts about nutrition research, as it pertains to milk and milk products.

One single milk vitamin, B_2, takes one of its commonly used names, *Lactoflavin,* from the source from which it first was isolated. This vitamin, discussed in this issue, may be regarded as typical of the many vitamin factors for which milk and milk products are valued by millions.

Lactoflavin—a Milk Vitamin—in Human Nutrition

The development over a period of years of the present understanding of the function of and necessity for adequate levels of Lactoflavin in human diets is a significant example of a major phase of nutrition research that began with milk and returns to milk as a basic dietary component.

One of the earliest series of research investigations of the Vitamin B complex, of which Lactoflavin is a member, was initiated in the 1920's by Dr. G. C. Supplee and associates. Dr. Supplee is director of the Borden Biological and Chemical Laboratory, located at Bainbridge, N. Y., which has maintained a leading part in the further breakdown of the B complex, now identified as to several members.

As pointed out by Dr. Supplee (1) in an article in Industrial and Engineering Chemistry:

> The status of milk as a food and especially as the sole diet of the very young necessarily implies that it contains all of the entities essential to sustain life and promote growth.

Consequently, the earliest investigations of vitamins were concerned largely with milk and various fractions of milk. Dr. Supplee, describing investigations into the water-soluble portion of milk, states:

> The first investigations relating to the vitamin activity of this material were carried out in the early twenties when knowledge of these dietary essentials was substantially limited to the fat-soluble and water-soluble classification; also, methods of study lacked the precision inherent in many of the biological methods perfected since that time. Nevertheless the results obtained from the inclusion of small amounts of this concentrated water-soluble milk fraction, in basal rations purified by the best means then available, were so conclusive in yielding evidence of a high concentration of vitamins that systematic investigations with improved methods have proceeded continually since that time.

Growth-Promoting, Life-Sustaining Substances Discovered in Milk

Dr. Supplee's article relates early experiments indicating that the water-soluble whey portion of milk contains growth-promoting factors of remarkable biological value:

> One of the striking early experiments was somewhat elementary. A basal ration was compounded with the gross components of milk, butterfat, casein, and lactose, further fortified with minerals and cod liver oil. Animals receiving this mixture failed to grow, became emaciated, and died within a few weeks. Other animals receiving the same basal mixture to which was added a small percentage of the concentrated whey fraction grew at a phenomenal rate and remained in good condition during observation periods of several weeks or months. This evidence was adequate to prove that growth-promoting and life-sustaining substances inherent in milk could be segregated from the gross components and retain a high degree of activity.

Factors for Growth Promotion Prominent in Milk

Discovery of these nutritive elements in milk laid the foundation for parallel investigations into the corresponding nutritive values of many other food products. Dr. Supplee's article points out that such investigations have made possible extraordinary results in promoting growth:

> These results invited comparison with other products known to contain the water-soluble vitamins. It was determined that basal rations containing from 7 to 12 per cent of the crude milk vitamin fraction promoted growth as satisfactorily as an equivalent amount of dry yeast . . . and also permitted reproduction, lactation, and normal rearing of the young. As the nature of the vitamin B complex became better understood, more detailed studies of the milk fraction were necessary. It was revealed that, even though it contained all water-soluble factors, some were present in greater amounts than others. . . .
>
> In developing the evidence concerning the vitamin characteristics of the concentrated whey fraction, it has been necessary to rechart or establish new objectives from time to time as improved techniques and further knowledge of the mode of action and chemistry of the vitamin entities became known. Increasing familiarity with the properties and limitations of the material has permitted the demonstration of some phenomenal results in the matter of growth promotion and control.

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Practically all Known Dietary Factors are in Milk

Continuation of these investigations over a period of many years showed that growth, health and reproduction of experimental animals on simplified experimental diets all were maintained or improved by the addition of portions of the water-soluble part (from whey) of milk. Dr. Supplee summarizes the significant general conclusion to be drawn from these investigations as follows:

> The evidence presented in regard to the vitamin value of whey obviously demands a more detailed consideration of the particular entities involved. Direct experimental data have shown the following factors to be present in whey or in the concentrated fraction previously described: lactoflavin (riboflavin vitamin B_2 or G), thiamine (vitamin B_1), the antiacrodynia factor (vitamin B_6), prothrombin (vitamin K), provitamin D (ergosterol or other antirachitically activable substances), the oestrogenic hormone, and obviously by permissible deduction, vitamin E and factor W. In brief, probably all known vitamins or other unidentified dietary essentials are present in whey to a greater or less degree; otherwise maintenance, growth promotion, and reproduction directly attributable to the concentrated fraction would be impossible.

The Borden research investigations into the vitamins of milk represented but a small portion of the total world-wide research conducted on these nutrition factors. Basic investigations, however, were centered largely on whey.

Vitamin B_2 Nomenclature

The history of investigations into Lactoflavin and the significance of nomenclature used in connection with this factor are told by Lela E. Booher (2) in the U. S. Department of Agriculture's comprehensive 1939 Yearbook, Food and Life:

> Riboflavin is now the generally accepted name for the water-soluble, yellow-pigmented vitamin that occurs in a wide variety of natural foods. In years past this vitamin has been designated by a number of different names, including lactoflavin, vitamin G, and vitamin B_2 — the last by English and German investigators. "Flavin" is derived from the Latin word "flavus," meaning yellow; the ending "in" implies that these yellow pigments contain nitrogen. The prefix "ribo" (or "d-ribo") identifies riboflavin as a particular member of this class of pigments that contains also the residue of a particular sugar, d-ribose. . . .
>
> The first scientific account . . . of the water-soluble yellow pigment in milk appeared in 1879. Not until almost 50 years later did this pigment again receive scientific consideration. Its more obvious properties were described in 1925 . . . but its real significance remained obscure until about 5 years ago.
>
> Independently and almost simultaneously, in 1933, American . . . and European . . . investigators announced the discovery of the biological significance of this pigment.

TECHNOLOGY

Vitamin Identified by Eliminating other Factors

The prominent part that milk played in the early work on all vitamins, and how Lactoflavin ultimately was isolated from milk and other products by a

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process of elimination is outlined in the Yearbook of Agriculture article:

> Early attempts to rear animals on a diet of purified protein, fat, carbohydrates, and inorganic salts met with complete failure. But if to this diet were added small quantities of milk whey and butterfat, the animals began almost immediately to grow and to show every appearance of being well nourished. It required nearly 20 years of active research before it became known that the water-soluble yellow pigment in whey was one of the vitamins that contributed to the successful rearing of animals on a simplified diet.
>
> Step by step the proteins, lactose, fats, and inorganic salts in whey were eliminated, leaving at each step a product more intensely yellow and more concentrated in vitamin activity. . . . Riboflavin was first isolated in pure crystalline form from egg whites by Kuhn and his coworkers. . . . Isolation of riboflavin from milk and many other plant and animal sources quickly followed as a result of the work of many investigators.

Human Need for Lactoflavin Established

The need by human beings for adequate levels of Riboflavin supplied in a liberal and well balanced diet to maintain normal health and prevent or alleviate specific deficiency disorders has been fully established (3, 7, 8, 9, 10, 11, 12).

Five years or more ago Lactoflavin emerged from the laboratories as a vitamin known and proved by experiment to be essential in *animal* nutrition. Biologists well understood that many of their findings about the physiological role of this vitamin in the nutrition of their laboratory test animals could be translated directly to human nutrition, but definite and certain proof, independent of inference, awaited careful clinical experiments and observation which, as forecast by early investigators, have recently established the following facts:

1. Milk is the most important source of Riboflavin in the human diet (2, 4, 5, 6). One quart of milk supplies 85% or more (4) of the tentatively accepted daily minimum adult requirement (4, 6).

2. Because of the multiple nature of naturally occurring Vitamin B complex deficiencies (7, 8), and because of the limitations of nutritive substances in pure chemical form (8, 9), foods naturally rich in the entire B complex are essential (7, 8, 9) to maintain health and alleviate deficiencies. Improvement is much more striking and permanent if persons suffering severe B complex avitaminoses are maintained on a well-balanced and liberal diet at least one-half of which should consist of milk, lean meat, and eggs (7).

3. Specific lesions attributed to ariboflavinosis, both experimentally and naturally occurring, in human beings include the following:

   Eye Disorders (3, 7)—Keratitis (inflammation of the cornea); itching, burning, and roughness of the eyes; photophobia (inability to tolerate light), dimness of vision in poor light, and partial blindness.

Lip and mouth conditions (Cheilosis) (3, 8, 10, 11) — Reddened, shiny, denuded lips, with maceration and fissuring in the angles of the mouth.

Tongue condition (Glossitis) (3, 10) — Purplish-red color and flattened papillae of tongue.

Skin condition (Seborrheic Dermatitis) (3, 8, 10, 11)—Accumulation of greasy scales on the skin, especially about the folds of the nose and mouth, and also, in some cases, around the ears and the eyelids.

4. Experimentally controlled diets (8, 12) deficient in Riboflavin, have produced in human beings specific clinical symptoms (ariboflavinosis) which are alleviated by administration of Riboflavin, but which are not relieved by other factors of the B complex (Nicotinic Acid and B_1).

5. Natural (as contrasted with experimentally induced) ariboflavinosis has been encountered by physicians in both the southern (8, 10) and northeastern (11) parts of the United States, who conclude that ariboflavinosis is probably a common dietary deficiency disease in some sections.

Lactoflavin an Essential Factor in Protecting Human Eyesight

Perhaps one of the most striking demonstrations of the necessity for Lactoflavin in the human diet is seen in the recent findings by United States Public Health Service research workers (3) that Lactoflavin is one of the essentials for protecting human eyesight. The symptoms of eye disorders resulting from Lactoflavin deficiency are itching, burning, pain or discomfort in bright light, and in a few cases, dimness of vision or partial blindness. The eye disorders in the several patients reported were accompanied by symptoms of other deficiencies, including pellagra, avitaminoses A and C, neuritis, anemia, and nutritional edema. Administration of Nicotinic Acid, Vitamin B_1, Vitamin C, Vitamin A, and Vitamin D had alleviated these symptoms but the disorders caused by Lactoflavin deficiency, including the eye disease, were benefited only by an adequate Lactoflavin intake.

Most Important Source of Lactoflavin in the Human Diet

What do these findings regarding the necessity for Lactoflavin mean in terms of milk and its place in the diet?

Milk is recognized as the most important source of Riboflavin in the human diet, according to Kunerth and Riddell (4), Sherman (5), and Sherman and Lanford (6).

Dr. H. C. Sherman (5) stated that:

> When account is taken of the amounts ordinarily eaten in reasonably well balanced dietaries and food supplies, milk is doubtless the most important source of vita-

min G for the American and European peoples. Breadstuffs and other bakery products can be much enriched in this vitamin by the incorporation of liberal amounts of milk or milk powder, whole or skimmed. Cream and ice-cream may be expected to contain about two-thirds to three-fourths as much vitamin G as an equal weight of fresh milk.

Milk—Logical Source of Lactoflavin

Both because of their naturally high Lactoflavin content and because of their widespread availability and universal use in the daily human diet milk and milk products are recognized as the primary practical source of this vitamin as compared with other sources. This subject is discussed by Sherman and Lanford (6) in The Journal of the American Medical Association:

> The relative amounts of riboflavin in foods are . . . a matter of importance to health and should be given weight in present-day considerations of food values and planning of the dietary. . . .
>
> . . . in milk as ordinarily produced under present-day conditions of dairy farming seasonal variations of vitamin vaiue are much smaller than would be inferred from many of the statements in the literature. Perhaps the best present evidence in this case is expressed in the figures of the seventeen available quantitative results of ten independent investigations. These show an average of 67 ± 3 Bourquin-Sherman . . . units of riboflavin per hundred grams of milk, with a coefficient of variation of 28, which is a lesser variability than would perhaps have been expected. Nor should there be any serious dimunition of the riboflavin value of milk in pasteurization or in preservation by drying or by condensation (partial evaporation) and canning. Milk is thus a relatively stable and dependable source of riboflavin and will almost always be the chief source in the dietaries of children because of the prominence that should be given to milk in the dietary for other nutritional reasons as well. In any long view of food economics there is also the consideration that milk is a food crop the production of which can be greatly increased in response to consumer demand, with little if any increase in cost per unit to the consumer.

Scientific literature frequently mentions liver and other products as sources of Riboflavin in experimental diets. The place of many such products in the human diet, however, is regarded as of lesser magnitude than that of milk as a practical source of Lactoflavin. Questions of price, availability, and similar considerations leave milk depended upon as the most significant source of Lactoflavin in practical human diets. This point is discussed by Sherman and Lanford (6):

> A contrasting case in this respect is that of liver, the supply of which can be increased only by rearing and slaughtering whole animals of which the liver is only a very minor part. Hence (as Minot, if we remember correctly, has complained) any emphasis on liver as a food for people in general has the unfortunate result of increase in its cost to those who really need it.

Dietary Requirement for Riboflavin

Sherman and Lanford (6) discuss the amounts of Lactoflavin that are essen-

tial and that can be utilized in human nutrition as follows:

> As yet, estimates of the amounts of riboflavin required for normal human nutrition are necessarily matters of judgment rather than of actual direct measurement. The independent judgments of Rose . . . and of Stiebeling . . . are in substantial agreement and are probably the most influential estimates thus far available. Rose has suggested for children up to 10 years of age at least 400 units a day in all cases, or 20 units per hundred calories if more than 2,000 calories a day is consumed; for adults, 20 units per hundred calories. The recommendation of Stiebeling is 450 units for boys under 6 and girls under 7 years of age, 540 units for boys from 7 to 10 and girls from 8 to 13 years of age, and 600 units for older children and adults, or 570 units per capita of the population.
>
> How far above these allowances the actual optimum will be found is a question for the future.

Regarding this latter point, the same authors (6) elsewhere in the article state:

> It is doubtless true, as suggested by Eusterman and Wilbur . . . "that certain individuals, the poor in particular, do not consume enough foods that contain (significant amounts of) vitamin A and vitamin G to insure a state of nutrition essential to the greatest physical stamina, efficiency and ability to resist infectious diseases." In fact, this view is strongly reenforced by the experimental finding . . . that the optimal intake of vitamin G (riboflavin) is very much (probably at least fourfold) higher than is easily demonstrable as strictly necessary.

Kunerth and Riddell (4) found from observations on the Lactoflavin content of cow's milk that the content of this vitamin is fairly uniform and that a pint of milk daily in the diet would furnish nearly half the normal adult requirement for Lactoflavin. A quart of milk would provide approximately 85% of the adult requirement.

Always Essential for Health

The need by large sections of the nation's population for improved nutritional standards, as emphasized by many public health workers and nutrition authorities, is one that is recognized by the entire milk industry. It long has been a major objective of leading nutrition authorities and continues to be a matter of governmental concern to improve the national nutritional status of all classes and all ages, by increasing general understanding and active application of the fact that for maintenance and protection of health diets liberally supplied with milk and milk products are essential.

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